REMARKS

I. Preliminary Remarks

Claims 9-13, 22 and 41 are amended herein and new claims 45-47 are added. Claims 8, 14-21, 23-40 and 42-44 are canceled. Support for new claims 45-47 can be found throughout the application as filed. Support for methods of diagnosing a neoplastic disease can be found, for example, pages 24-27. Support for the effects of unprocessed VEGF-D on the growth characteristics of a neoplastic disease can be found, for example, in Example 9 (and, in particular, paragraph [0153]). Support for measuring the amount and size of VEGF-D in a sample can also be found in Example 9 (and, in particular, paragraph [0148]). Support for the various types of samples recited in claim 46 can be found in paragraph [0057]. Accordingly, no new matter has been added by the amendments made herein.

Applicants reserve the right to pursue the subject matter of any canceled claim in continuing applications.

II. The rejection under 35 U.S.C. § 112, second paragraph, should be withdrawn.

The Examiner rejected claims 8-27 and 36-44 as assertedly being indefinite. In particular, the Examiner asserted that independent claims 8, 14, 18, 23, 36 and 40 are incomplete method claims for missing steps for detecting unprocessed VEGF-D. The rejection is moot in view of the cancellation of these claims. New claim 45 recites steps for measuring the VEGF-D polypeptide in the sample.

In the office action, the Examiner asserted that, "In order to detect unprocessed versus processed VEGF-D., the size of VEGF-D in the sample must be determined." (Office action at page 2.) New claim 45 specifically recites determining both the amount and the size of the VEGF-D.

The Examiner also asserted, "Histochemistry does not detect the size of the VEGF-tD fragment." (Office action at page 2.) The applicants respectfully disagree. For example, by subjecting a sample to electrophoresis or other size separation techniques,

histochemistry can be used both to quantify and to measure the size the protein of interest. To provide just one example technique, a Western blot is useful for assessing both size and quantity of a protein of interest, such as VEGF-D. The present application discloses the use of such a technique to assess the size of VEGF-D. See, for example, Example 9 (and, in particular, paragraph [0148]) and Example 13.

The Examiner also asserted that the claim should have a control "which enables one of ordinary skill in the art to compare to and arrive at the conclusion that the level of unprocessed VEGF-D is increased in cells obtained from an organism suspect of being in a neoplastic disease." New claim 45 specifies measuring both the amount and the size of the VEGF-D. The application enables a person of ordinary skill to draw the proper conclusion from these two measurements. Comparison of the amount and size of the VEGF-D to a control is one option, but is not the only technique enabled by the application.

Thus, new claim 45 renders moot all of the reasons for the rejection.

III. The rejection under 35 U.S.C. § 102(b) should be withdrawn.

The Examiner rejected claims 8-11 and 13 under 35 U.S.C. § 102(b) as allegedly being anticipated by WO 98/07832 ("Achen I"). Applicants request reconsideration of the rejection in view of the amendments made herein and the following remarks.

The present application discloses that tumors expressing increased amounts of ***unprocessed*** (i.e., full-length) VEGF-D leads to faster tumor growth and increased metastatic risk than tumors expressing other forms of VEGF-D (i.e., fully processed or truncated portions of VEGF-D). See, Example 9 of the present application.

The Examiner asserts that Achen I anticipates the pending claims because Achen I discloses methods of detecting VEGF-D in a sample and antibodies that bind to unprocessed VEGF-D. Applicants disagree. Even if Achen I generically discloses methods of detecting VEGF-D in a sample and methods of screening for cancer associated with VEGF-D, it does not specifically disclose or suggest measuring both the amount and <u>size</u> of the VEGF-D or diagnosing the growth characteristics of a neoplastic disease based on the amount of ***unprocessed*** VEGF-D in a sample. Achen I also does not specifically disclose

that tumors expressing ***unprocessed*** VEGF-D generate more blood and lymphatic vessels than tumors expressing other forms of VEGF-D. The present application is the first disclosure of the association between the amount of ***unprocessed*** VEGF-D and the intensity of the resulting tumors.

Because Achen I does not specifically disclose methods of screening for a neoplastic disease characterized by an increase in the amount of ***unprocessed*** VEGF-D in cancers, it cannot anticipate any of claims 8-11 and 13. Anticipation requires that the cited art disclose each and every element of the claims, which is not the case here.

The Examiner further asserts that the recitation of increased amounts of unprocessed VEGF-D is an inherent characteristic of cancer. Applicants disagree. As summarized in MPEP 2112, "the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic." (Emphasis in original) In re Rijckaert, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993), In re Oelrich, 666 F.2d 578, 581-582, 212 USPQ 323, 326 CCPA 1981). The Examiner has not provided any evidence to suggest that all cancers (regardless of severity) express increased amounts of ***unprocessed*** VEGF-D. The correlation between increased amounts of ***unprocessed*** VEGF-D expression and tumor severity is unique to the present application. Therefore, there is insufficient evidence to conclude that all cancers express increased amounts of ***unprocessed*** VEGF-D. The Examiner is reminded that "inherency . . . may not be established by probabilities or possibilities." *See Purdue Pharma v. Boehringer Ingleheim 98 F.Supp. 2d 362, 379 (SDNY, 2000), citing Mehl/Biophile Int'l Corp., 192 F.3d at 1365).*

Moreover, even if increased amounts of unprocessed VEGF-D were an inherent characteristic of *some* tumors, this fact would have no bearing on the novelty of the current claims. After all, the current claims are not directed to the tumors themselves. The current claims are directed to a method that includes steps that direct an analysis of the unprocessed VEGF-D. The prior art relied upon by the Examiner as allegedly being anticipatory does *not* disclose or suggest such method steps. Allegedly inherent features of a tumor do not destroy the novelty of a method claim.

In view of the foregoing, applicants respectfully request that the rejection of claims 9-11 and 13 (claims 8 is canceled) under 35 U.S.C. § 102(b) be withdrawn.

IV. The rejections under 35 U.S.C. § 103(a) should be withdrawn.

A. Claims 8, 12, 14-21 and 36-44 are patentable over WO 98/07832 and WO 99/33485.

The Examiner rejected claims 8, 12, 14-21 and 36-44 under 35 U.S.C. § 103(a) as allegedly being unpatentable over WO 98/07832 ("Achen I") and WO 99/33485 ("Achen II"). Applicants request reconsideration of the rejection in view of the following remarks.

To establish a *prima facie* case of obviousness, "the prior art reference (or references when combined) must teach or suggest all the claim limitations." M.P.E.P. § 2143. The cited art fails to disclose or suggest all claim limitations. As discussed above in Section III, Achen I does not specifically disclose or suggest a method of diagnosing the growth characteristics of a neoplastic disease based on the amount of ***unprocessed*** VEGF-D in a sample. Achen II fails to remedy the deficiencies of Achen I. In particular, Achen II also does not specifically disclose or suggest a method of diagnosing the growth characteristics of a neoplastic disease based on the amount of ***unprocessed*** VEGF-D in a sample. Moreover, because neither Achen I nor Achen II correlates a neoplastic disease (or metastatic risk) with increased amounts of ***unprocessed*** VEGF-D, one of skill in the art would not have a reasonable expectation of success for arriving at the claimed invention.

Because the cited art, either alone or in combination, does not disclose or suggest each element of the claims (i.e., a method of diagnosing the growth characteristics of a neoplastic disease based on the amount of ***unprocessed*** VEGF-D in a sample) and because the lack of such a disclosure does not provide one of skill in the art with a reasonable expectation of success for arriving at the claimed invention, the Examiner has failed to establish a *prima facie* case obviousness. Accordingly, the rejections of claim 12 (claims 8, 14-21 and 36-44 are canceled) under 35 U.S.C. § 103(a) should be withdrawn.

B. Claims 22-27 are patentable over the cited art.

The Examiner rejected claims 22-27 as allegedly being unpatentable over Achen I in view of Achen II and further in view of Achen et al. (Proc. Natl. Acad. Sci. USA, 95:548-553, 1998; ("Achen III")), and Valtola et al. (Am. J. Pathol., 154:1381-1390, 1999; ("Valtola"), or Salven et al. (Am. J. Pathol., 153:103-108, 1998; ("Salven"), or Tsurusaki et al. (Br. J. Cancer, 80:309-313, 1999; ("Tsurusaki"). Applicants request reconsideration of the rejection in view of the following remarks.

As discussed above in Section III and Section IV, part A, the disclosures of Achen I and Achen II, either alone or in combination, fail to disclose or suggest the diagnosing methods recited in the claims. None of the supporting references relied on by the Examiner for this rejection remedy the deficiencies of Achen I and Achen II. In particular, none of the cited art discloses or suggests a method of diagnosing the growth characteristics of a neoplastic disease based on the amount of ***unprocessed*** VEGF-D polypeptide in a sample. Moreover, none of the cited art correlates an increased amount of unprocessed VEGF-D expression with a neoplastic disease state (or metastatic risk).

Because the cited art, either alone or in combination, fails to disclose or suggest each element of the claims (i.e., a method of diagnosing the growth characteristics of a neoplastic disease based on the amount of ***unprocessed*** VEGF-D polypeptide in a sample) and because the lack of such a disclosure does not provide one of skill in the art with a reasonable expectation of success for arriving at the claimed invention, the Examiner has failed to establish a *prima facie* case obviousness. Accordingly, the rejections of claim 22 (claims 23-27 are canceled herein) under 35 U.S.C. § 103(a) should be withdrawn.

V. The obviousness-type double-patenting rejection should be withdrawn.

The Examiner rejected claims 8-27 and 36-44 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 6,730,489 (hereinafter "the '489 patent"). Applicants disagree.

The Examiner asserts that the '489 patent anticipates the present claims because claims 1 and 2 of the '489 patent recite methods of detecting VEGF-D in a sample and antibodies that bind to VEGF-D. Even if the Examiner has properly characterized the issued claims, the rejection is improper. New claim 45 is directed to a method of diagnosing growth characteristics of a neoplastic disease comprising, in part, measuring the amount and size of the VEGF-D and diagnosing the growth characteristics of the neoplastic disease based on the amount of ***unprocessed*** VEGF-D in a sample. The '489 patent is silent with respect to such a method and therefore cannot anticipate any of the claims presented herein.

The Examiner further asserts that claims 1-20 of the '489 patent, in combination with the disclosures of Achen III, Valtola, or Salven or Tsurusaki, anticipate the pending claims. Applicants disagree. As discussed above, the '489 patent does not recite the method of new claim 45 in its claims. None of the supporting references relied on by the Examiner for this rejection remedy the deficiencies of the '489 patent. In particular, none of the cited art discloses or suggests a method of diagnosing the growth characteristics of a neoplastic disease based on the amount of ***unprocessed*** VEGF-D in a sample. Moreover, none of the cited art correlates an increased amount of unprocessed VEGF-D expression with a neoplastic disease state (or metastatic risk). Because the cited art, either alone or in combination, fails to disclose or suggest each element of the claims (i.e., a method of diagnosing the growth characteristics of a neoplastic disease based on the amount of ***unprocessed*** VEGF-D polypeptide in a sample) and because the lack of such a disclosure does not provide one of skill in the art with a reasonable expectation of success for arriving at the claimed invention, the Examiner has failed to establish a *prima facie* case obviousness.

In view of the foregoing, the double patenting rejection is improper and should be withdrawn.

VI. Conclusion

For the foregoing reasons, Applicants request withdrawal of all outstanding rejections and allowance of the pending claims. No other fees are believed to be due with the filing of this paper. However, the Director is authorized to charge any additional fees deemed necessary to Deposit Account No. 13-2855, under order number 28967/5680D.

If the Examiner believes that a telephone conversation would expedite allowance of the claims, she is invited to contact the undersigned agent or David A. Gass, attorney for applicants, at the number below.

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Respectfully submitted,

By: /Jeanne M. Brashear/56,301
Jeanne M. Brashear
Registration No.: 56,301
MARSHALL, GERSTEIN & BORUN LLP
233 S. Wacker Drive, Suite 6300
Sears Tower
Chicago, Illinois 60606-6357
(312) 474-6300
Agent for Applicants